Sensory information from afferent neurons

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PROGRESS REPORT #3

for the period

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I. Objectives of Overall Project

Our aim is to develop and perfect, in an animal model, methods for chronic recording and processing of afferent activity produced by sensory receptors that could yield information about human fingertip contact, grasped object slip, finger position, and grasp force applicable for restoration of motor functions in the paralyzed human hand. The specified contract objectives are:

1. Select recording methods that:
   a. Have the potential of providing safe, reliable recordings in humans for periods of years.
   b. When used in human applications, could provide relatively isolated information from the sensory endings in the thumb pad and in the finger pads of the second and third fingers.
   c. Could, in human applications, provide information from the proprioceptive receptors in the muscles of the hand and wrist.

2. Select an animal model suitable for chronic recording of afferent nerve activity, and give consideration to modeling electrode placement sites for a potential human neural prosthesis application.

3. Fabricate or obtain chronic electrodes and associated cables and percutaneous connectors for chronic recording of sensory afferent activity.
   a. Design electrodes and cables using biocompatible materials that would be suitable for potential future human implants.
   b. Design electrodes and cables with the goal of producing a chronic implant that causes minimal nerve damage.

4. Investigate the possibility of extracting information about contact, grasped object slip, limb position and contact force from chronically recorded neural activity using the animal model and electrodes from parts 2 and 3.
   a. Devise recording, processing, and detection methods to extract this information from recorded neural activity in a restrained animal.
   b. Modify these methods as needed to function in an unrestrained animal and in the presence of stimulation artifacts associated with functional electrical stimulation.
   c. Record activity for periods of at least 6 months and devise functional measures to track any change in neural response over this time.
   d. Evaluate any histological changes in the nerves that occurred over the period of chronic recording and, if possible, correlate these changes to changes in functional response.

5. Cooperate with other investigators in the Neural Prosthesis Program by collaboration and sharing of experimental findings.

II. Summary of Progress in the Third Period

During the third reporting period we completed the six chronic implants planned for the first year of this contract. We implanted three new animals, one with Multi-Contact Cuffs (MCCs) and two with Longitudinal Intrafascicular Electrodes (LIFEs). We periodically monitored compound action potentials and device impedances under anesthesia from all six implants, and we monitored trends in selectivity with multi-channel recordings (MCCs and LIFEs) using electrical stimulation and mechanical stimulation of the digits. We developed new techniques of obtaining useful data and parameters from asynchronous ENG data during mechanical perturbations, and we constructed and tested a five digit manipulator that is capable of producing both slips and normal perturbations on each digit. Our first chronic implant reached the end of the 180 day monitoring period.

III. Details of Progress in the Third Period

A. Long-term stability of Compound Action Potentials and Devices

During the third reporting period, we implanted three more animals for long term evaluation of device longevity and stability of the instrumented nerves. We implanted one cat with Multi-Contact Cuffs (MCCs) and two cats with Longitudinal Intrafascicular Electrodes (LIFEs) on the Median and Ulnar nerves as discussed in PR#2. This brought our total number of chronic implants to six animals: three MCC implants and three LIFE implants.

Table 1 presents an update of the status of the six implants. The table shows the implant type, the last recording day prior to this report, the status of the Median and Ulnar nerves as a percentage of the day 0 nerve Compound Action Potential (CAP) amplitudes (recorded with tripolar circumferential electrodes), and the status of the CAPs measured with MCC internal electrodes or LIFEs as a percentage of day 0. The MCC and LIFE CAP values shown are the average (± 1SD) of the four bipolar channels recorded from that particular nerve.

In general, the Median and Ulnar nerves in each implant have remained healthy as shown by the whole nerve CAPs recorded with circumferential electrodes. The reason for the low CAP amplitude for the Ulnar nerve in NIH 18 is that the wires to the Ulnar cuff were damaged during the implant surgery and now provide a single-ended, unbalanced ENG signal rather than a balanced tripolar signal (see PR#2 for more details). The range of amplitudes of tripolar CAPs recorded in the other animals is consistent with our previous series of long-term implants of conventional single-channel cuffs reported in our previous contract (NIH-NINDS-NO1-NS-3-2380).

Table 1: Status of six NIH implants as of Apr. 30, 1997

Subject	Implant Type	Last Rec. Day	Median Nerve Cuff CAP (% of day 0)	Ulnar Nerve Cuff CAP (% of day 0)	Average Median Nerve Internal Electrodes (%day 0 ± SD)	Average Ulnar Nerve Internal Electrodes (%day 0 ± SD)
NIH 18	MCCs	168	255%	11%	161% ± 47%	25% ± 12%
NIH 19	MCCs	126	103%	143%	76% ± 48%	69% ± 21%
NIH 20	LIFEs	134	45%	59%	26% ± 12%	40% ± 28%
NIH 21	MCCs	63	73%	86%	57% ± 8%	69% ± 11%
NIH 22	LIFEs	38	53%	137%	22% ± 8%	14% ± 11%
NIH 23	LIFEs	16	66%	122%	14% ± 6%	45% ± 33%

As time progressed, the three animals implanted with MCCs tended to show smaller declines in the localized CAP amplitudes than the three animals implanted with LIFEs. Connective tissue ingrowth into the MCCs may have resulted in decreasing localized CAP amplitudes. Generally, the internal electrode CAPs paralleled the trends in whole-cuff circumferential electrode CAPs.

The LIFE CAP amplitudes generally dropped significantly in the first two to four weeks after implant and then leveled out at values ranging from 10% to 45% of the day 0 CAP amplitudes. The mechanism for this drop is likely to be progressive tissue encapsulation of the electrodes inside the nerve and subsequent shielding of and distancing from the electrode and the signal source.

Histological investigation of these implants will investigate the extent of MCC and LIFE electrode encapsulation after six months.

B. Trends in Signal to Noise Ratios with Compound Action Potential Recordings

A feature of the CAP recordings that we are tracking is the signal to noise ratio (SNR) of ENG to EMG. In each recording, we stimulate the proximal cuff on the Median or Ulnar nerve and record the evoked CAP with the distal tripolar recording cuff as well as the MCC or LIFE devices, as detailed in our previous progress reports. Each signal from the distal devices includes an ENG component conducted down the nerve and an EMG pickup component which is produced by stimulated muscles near the nerve and the electrodes.

Figure 1 shows a typical example of CAP signals recorded with a tripolar cuff when a series of stimuli of progressively greater intensities was delivered at time zero. The typically triphasic nerve CAP normally occurs after 1 to 1.5 ms (for a conduction distance of approximately 10 to 15 cm) and the EMG component occurs later at about 2 to 5 ms.

We have defined the SNR of the recording device to be:

$$SNR = \frac{ENGpp}{EMGpp}$$

In Fig. 1, the SNR would be just under 1 as the ENGpp was slightly less than the EMGpp. The SNR value gives an indication about relative changes in the recording properties of the device, including fluctuations in the ENG amplitude and changes in the rejection of unwanted EMG contamination. In this NIH contract we are determining and comparing the SNR properties of the implanted devices (tripolar recording cuffs, MCCs, and LIFEs) over the length of the implant period.

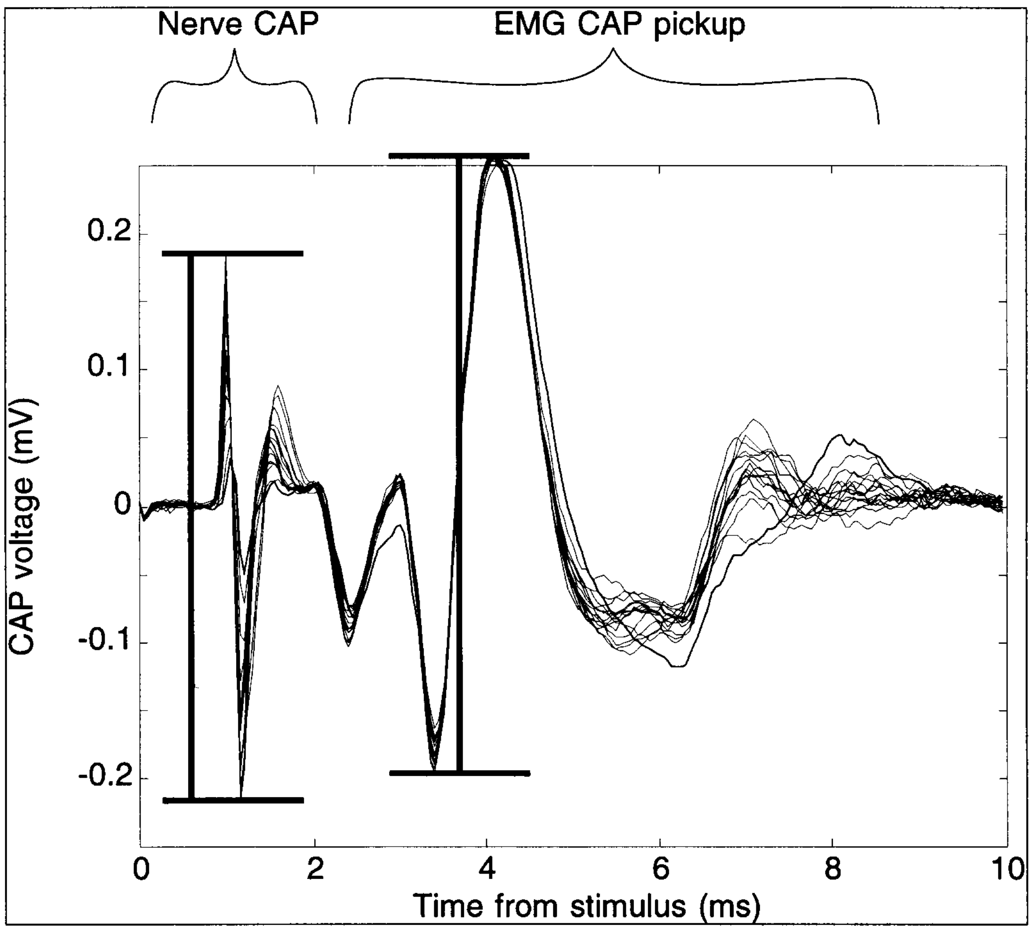

Figure 1: Example of CAP from a nerve cuff showing peak-to-peak measurements of ENG and EMG components of the signal. SNR R equals ENG peak-to-peak divided by EMG peak-to-peak.

Figure 2 shows the SNRs recorded thus far from these six implants. Each data point represents the average of eight SNRs from eight localized bipolar recording electrode pairs (either MCCs or LIFEs, with four electrode pairs on each of the Median and Ulnar nerves).

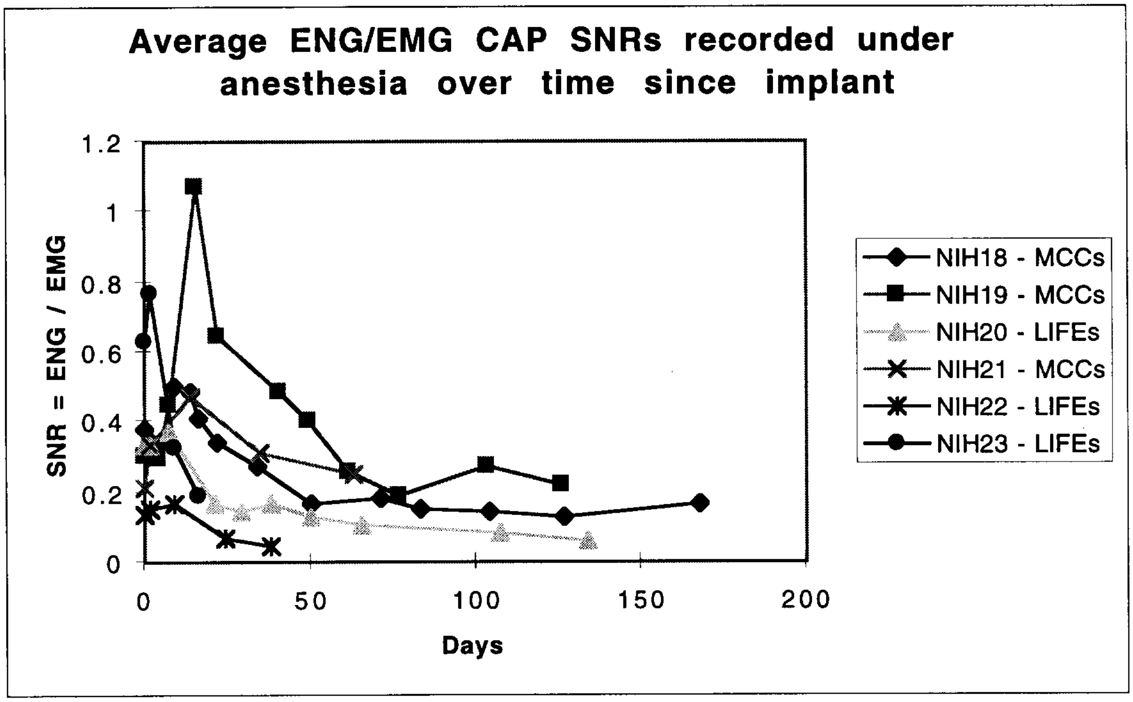

Figure 2: Trends in average CAP signal to noise ratios (SNR equals ENG peak-to-peak divided by EMG peak-to-peak) for each implant. Each data point represents the average of eight neural signals (i.e. 4 channels from the Median nerve and 4 channels from the Ulnar nerve) recorded during the same recording day. Data updated to Apr. 30, 1997.

Figure 2 shows that typically the MCCs had higher SNRs than LIFEs over the implant period. The MCCs appear to have better SNRs because they benefit from the EMG rejection characteristics of the surrounding silicone cuff wall. In general, the MCCs and LIFEs showed ENG signals of similar amplitude, so the main difference in the SNRs was their EMG rejection properties. A trend of decreasing SNRs over time was also seen with all the devices (MCCs and LIFEs) as the ENG signals decreased due to tissue encapsulation.

For comparison of relative performance, typical tripolar recording cuffs produce SNRs between approximately 1 and 3 as they benefit from having silicone cuff wall shielding and a balanced tripolar electrode configuration.

Figure 3 shows the same data presented in Fig. 2, but as the averages of 4 signals from each individual Median or Ulnar nerve.

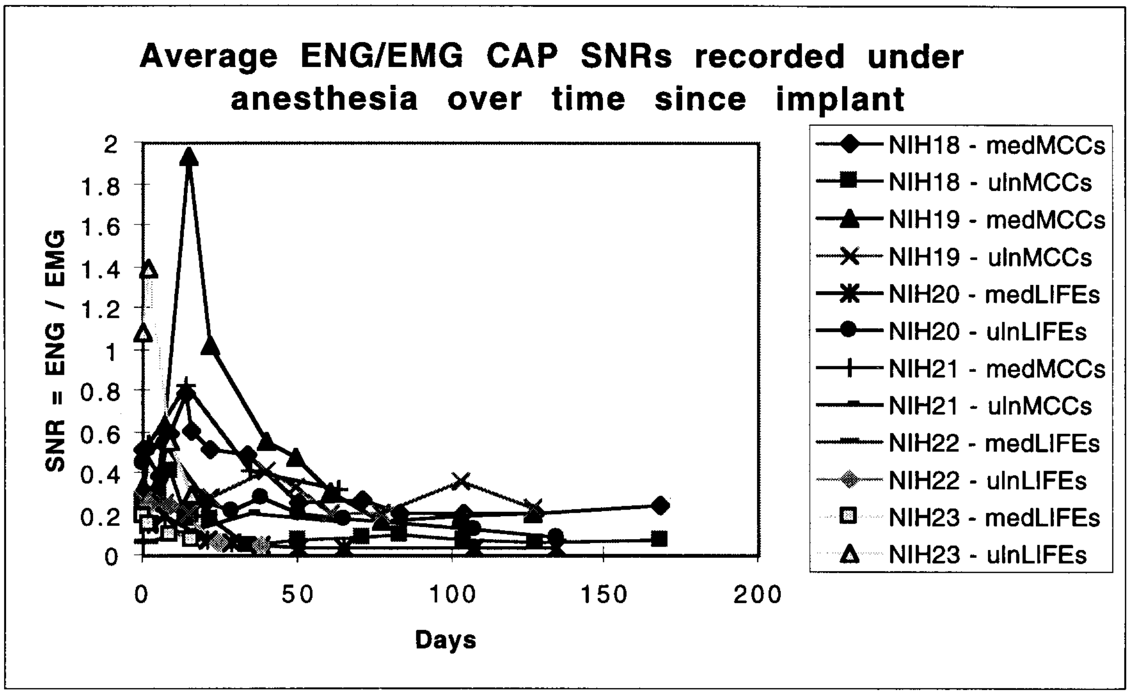

Figure 3: Trends in average CAP signal to noise ratios (SNR equals ENG peak-to-peak divided by EMG peak-to-peak) for each implant. Each data point represents the average of four neural signals (i.e. 4 channels from the Median nerve or 4 channels from the Ulnar nerve) recorded during the same recording day. Data updated to Apr. 30, 1997.

All of the devices demonstrated the same general trend of initially high SNRs followed by sharp decreases in SNR in the first 50 to 75 days and relatively stable SNRs for the remainder of the implant period. There appears to be some difference between devices implanted on the Median and the Ulnar nerves, with Median MCCs showing slightly higher SNRs in NIH18, 19, and 21 than Ulnar MCCs.

The implanted LIFEs showed similar trends of decreasing SNRs over time, with generally lower overall values We have been investigating methods of increasing LIFE SNR by decreasing EMG pickup through shielding. In NIH23, we wrapped the LIFE implant site on the Ulnar nerve with gold-sputtered Teflon. Initially this approach produced higher SNRs (see Fig. 3, NIH23-ulnLIFEs). After approximately three weeks, however, the SNR dropped to levels similar to other LIFE implants.

During these CAP recordings, all of the MCC and LIFE signals were bandpass filtered with single-pole filters at 500 Hz and 10 kHz. We selected this relatively wide open filtering window to allow considerable EMG to pass though and so evaluate the EMG rejection characteristics of the implanted devices without assistance from sharp filtering. In a clinical application, however, sharp highpass filtering would be advisable to increase EMG rejection and increase the SNR.

The longevity results with both the MCCs and LIFEs are encouraging and suggest that, even though the SNRs of these devices were less than for standard tripolar recording cuffs, useable ENG signals can be recorded over extended periods.

C. Trends in Selectivity to Electrical Stimulation of the Digits

Progress Report #2 detailed our protocols for data collection and analysis for experiments involving multi-channel selectivity with electrical stimulation of the digits. Each recording day produces a single overall "selectivity index" which is a relative metric of the effectiveness of the entire array of eight recording electrodes. We record a total of eight point-source ENG signals from either four pairs of LIFEs in both the Median and Ulnar nerves, or from two MCC with four localized bipolar electrodes each, placed on the Median and Ulnar nerves.

We are monitoring the selectivity indices to determine if trends develop over time that can be associated with trends in the recording parameters of the electrodes shown by CAP recordings and by impedances. Figure 4 presents data from the six chronic implants over their implant periods to date.

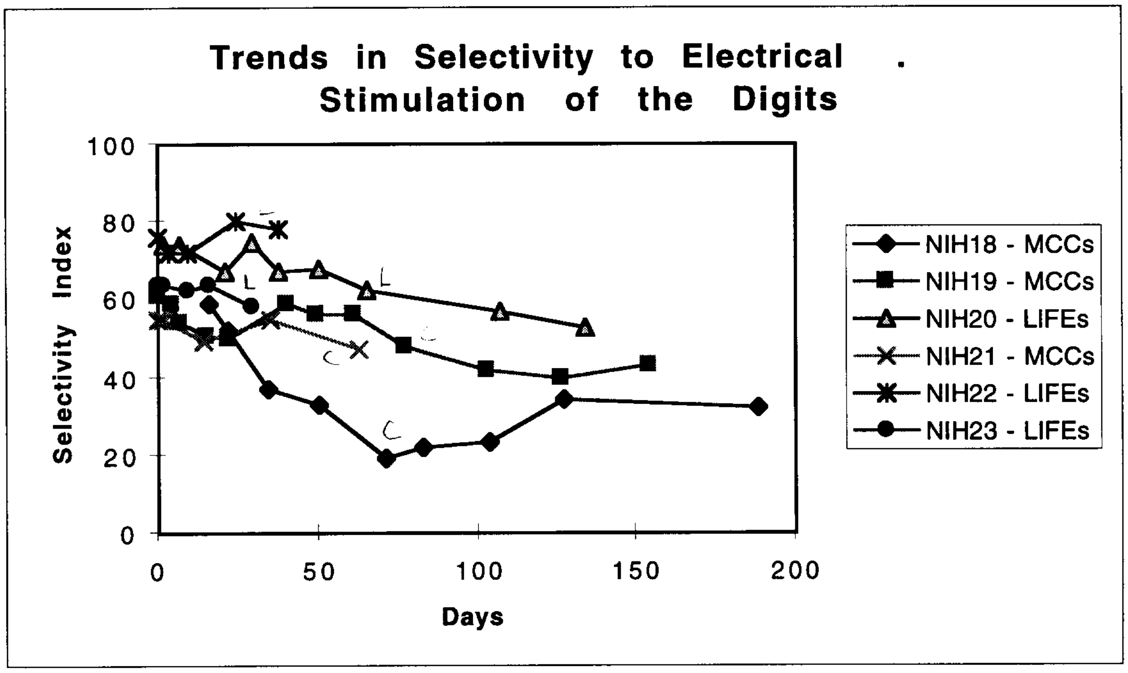

Figure 4: Trends in selectivity with electrical stimulation of the digits. Each data point represents the overall selectivity index recorded with the eight channel configuration (i.e. 4 Median ENG signals plus 4 Ulnar ENG signals) for each recording day. Data updated to May 7, 1997.

The preliminary results shown in Fig. 4 demonstrate that the arrays of LIFE electrodes generally produced higher selectivity indices than the MCCs for the electrical stimulation experiments. With electrical stimulation of each digit, in general, LIFE pairs show either a large evoked signal or no signal at all (other than background neural activity). LIFE electrodes thus give a nearly binary signal depending on whether they are situated near axons which innervate the stimulated digit.

In contrast, the four sets of localized electrodes in the MCCs, external to the nerve, produce signals which tend to have the same general shape but vary in amplitude presumably as a function of their distance from the signal source inside the nerve. With activity on all channels from a given set of electrodes, the MCCs do not produce the same type of vector separation between digits as produced by the LIFEs. The maximum selectivity index produced with LIFE electrodes was 80 (NIH22, day 24) and the maximum selectivity index produced with MCCs was 61 (NIH19, day 0).

The selectivity indices from both types of implants appear to drop initially, which can be attributed to decreases in CAP signal amplitude due to encapsulation (and possible migration in the case of LIFEs) and to decreases in device impedances. From our initial data, it appears that the selectivity indices stabilize after 75 to 100 days, which suggests that implanting arrays of these types of electrodes for improved sensory signal acquisition may be feasible for long term FES applications.

D. Selectivity Results with Digit Perturbations

1. Five-digit manipulator

The five-digit manipulator that we designed is now fully functional. A figure of the manipulator positioned below a subject's forepaw is shown below. The manipulator is capable of delivering either a slip perturbation along the long axis of the digit by energizing one of the outer solenoids, or a contact perturbation against the digit pad by energizing one of the inner solenoids.

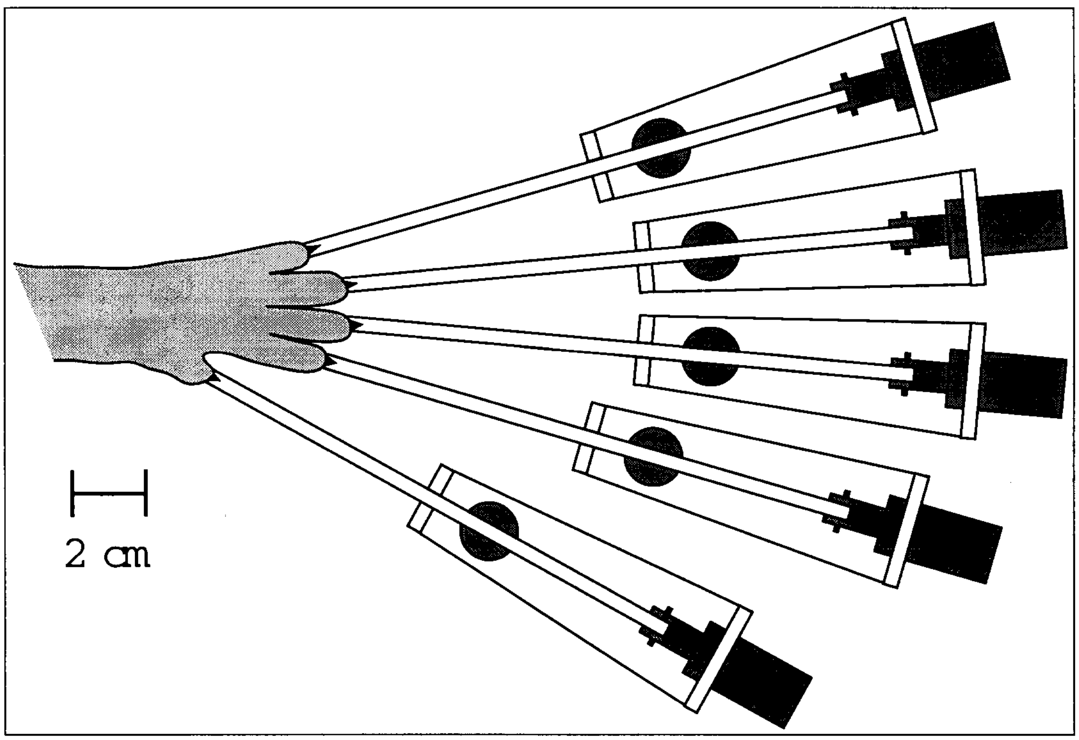

Figure 5: Schematic of the five-digit manipulator

The manipulator is computer-controlled and any sequence of individual perturbations may be applied to the digits. At the present time we have limited the experiments to either a series of slip perturbations or a series of normal perturbations that are applied to the digits sequentially at an average rate of about one perturbation per digit per second.

2. Selectivity analysis method

The following procedure was used to test responses to mechanical stimulation of digits.

The animal was anesthetized, the left forelimb was supported between elbow and wrist, and the manipulator was positioned under the forepaw digits. Neural signals arising from the electrode arrays in the Median and Ulnar nerves were amplified x100k, bandpass filtered between 500 Hz and 10 kHz, and recorded onto 20-channel FM tape. After recording began, the manipulator went through its programmed sequence of perturbations.

Until recently we could only record from one nerve's electrode array at a time since we had only four amplifiers available in the lab, so we ran an experiment while recording the Median nerve activity and then reran the same experiment while recording the Ulnar nerve activity. During the past reporting period, we designed and constructed 8-channel amplifiers and we began recording all of the data in parallel. This new recording scenario allowed us to make better recordings because all signals were recorded in parallel which allowed us to better monitor the intertrial variability. The variability was due to changes in the mechanical input to the digits and changes in mechanoreceptor responses.

After a given experiment was completed, the data stored on the FM tape was sampled, digitized and then stored on CD. Having these data in digital form allowed us to manipulate the data off-line with various software packages.

Due to the low amplitude and brief duration of the neural bursts that occur in the Median and Ulnar nerves when a mechanical perturbation is applied to one of the digits, some signal processing is necessary in order to obtain a useful signal for further analysis. This processing includes removing DC offset, rectifying the neural signal, and then low-pass filtering the signal at 400 Hz to obtain the envelope of the neural burst. Three features were then extracted from the signal: (1) the peak of the filtered neural burst, (2) the time from the onset of the perturbation to the peak of the neural burst, and (3) the area of the burst over baseline level, integrated over a 50 ms duration.

3. Selectivity results

Two features (peak and area) were used to carry out a selectivity analysis similar to the one used for the electrical stimulation of the digits. The results were comparable to the results from the electrical stimulation studies, with average selectivity values around 25 from peak analysis and 45 from area analysis. What may contribute to the poorer quality signals is the fact that averaging of features from the same digit was required and there was a large standard deviation that was not seen with the electrical studies. The large variability was probably due to the low signal to noise ratio that was seen with the neural bursts where the signal amplitude had a peak only about 4 times greater than the background activity.

We found that the neural activity occurring after slip perturbations produced slightly better results than that obtained from normal perturbations. This fact may be due to slip perturbations having a more localized effect that affects only one digit, whereas the normal perturbation may cause greater movement in the other digits and may cause confounding results.

4. Identification results

We have started to determine whether or not the perturbed digit can be identified from sets of neural signals. Using data from early trials, when only four data channels could be recorded at a time, we have looked at trying to identify either one of the first four digits based on the recorded signals from the Median nerve electrode arrays or one of the last two digits based on recorded signals from the Ulnar nerve electrode arrays. A discriminant function in the SPSS software package was used to classify a set of cases and compare the predicted digit to the actual perturbed digit. The result from this preliminary analysis is promising as the Ulnar innervated digits could be correctly identified in approximately 77% of trials for a MCC subject and 95% of trials for a LIFE subject. The median innervated digits were less easily identified, at approximately 54% for the MCC subject and 87% for the LIFE subject. Results for the full 8-channel, 5-digit trial analysis are forthcoming.

IV. Publications and Meetings

A. Publications

Six abstracts were accepted for presentation at the joint IFESS/NP5 Meeting to be held in Vancouver, Canada on August 16-21, 1997.

Copies of the abstracts are included in Appendix A.

V. Plans for the Fourth Period

During the fourth reporting period, from May 1, 1997 to Aug. 30, 1997, our objectives will consist of the following:

We will continue to monitor CAPs and device impedances under anesthesia until each of the six animals currently under study reaches the 180 day end point, and we will also continue to assess selectivity of recording during digit electrical stimulation and mechanical perturbation experiments under anesthesia. We will evaluate the perturbation selectivity data off-line to determine the feasibility of identifying the digit and mode of perturbation based solely on the ENG signals recorded with the LIFEs or the MCCs. As each implanted animal completes the 180 day implant period (most will occur in the fourth period), we will perform final acute experiments to retrieve devices and harvest nerve tissues for histological analysis.

We will collect data during walking on the treadmill and the multi-channel ENG data from the LIFEs and from the MCCs will be evaluated to determine if differences in the signals (and thus the selectivity) can be detected and to determine the reliability and utility of these signals.

We will continue the collaboration with Drs. Yoshida and Stein by monitoring the three animals currently implanted with LIFEs.

We will proceed with the collaboration with Dr. Andrews by collecting data from the MCCs and virtual sensors during experiments under anesthesia and during walking on the treadmill. In this period we hope to test the implantability of artificial sensors and to develop a footfall sensor to determine exactly when the cat paw touches the treadmill belt.

VI. Progress with Subcontractor Collaborations

A. B.J. Andrews, University of Alberta

In preparation for chronic implantation of artificial sensors in the forelimbs of cats at SFU, Dr. Andrews has proceeded with development and testing of external sensors designed with accelerometers at UofA. The overall aim of this subcontract is to directly compare the results of detecting the phases of gait with both natural and artificial sensors, and to investigate methods of retrieving and utilizing gait phase information from the data.

1. Detecting the Phase of Gait using Accelerometers

Accurate, real time detection of the main phases of human gait was achieved using supervised learning techniques and a set of three closely spaced accelerometers attached to the shank of three able-bodied student volunteers. The purpose of the present study was to investigate the feasibility of a gait phase predictor for use in future FES control systems to assisting hemiplegic or paraplegic ambulating, in which sensors are located in spatially discrete clusters. In implanted systems this may reduce the number of interconnected encapsulated packages; and in surface systems this may provide flexibility in locating devices unobtrusively.

The sensor cluster comprised three surface micro-machined silicon accelerometers (Analog Devices type ADLX05) attached on the shanks of 3 able bodied volunteers (Male, age 20 - 24, height 1.66-1.78 m, weight 66 - 86 kg). We detected the five gait phases previously reported (J. Perry, (1992) "Gait Analysis: Normal and Pathological Function" Thorofare, N.J. : Slack Inc.) and referred to as: loading response, mid-stance, terminal stance, pre-swing and swing. Supervised machine learning was used to synthesize the gait phase detector and also facilitated placement of sensors by removing any requirement for precise anatomical alignment. Two commercially available inductive learning algorithms were compared i.e. Rough Sets 1.3R by Reduct Systems Inc. and Adaptive Logic Networks v 3.0 by Dendronic Systems Inc. The prediction accuracy of the gait event detector was compared with a previous method reported for a clinically-used FES dropfoot orthosis for hemiplegics based on the use of an inclinometer and a hand crafted rule based stance-swing detector (Dai, R., Stein, R.B., Andrews, B.J., James, K.B., and Weiler, M. (1996), Application of tilt sensors in FES, *IEEE Trans Rehab. Eng.*, vol. 4, No. 2, 63-72.).

In order to provide known examples of the five gait phases an insole pressure sensor array and a hand crafted rule based discriminator were developed. These 'known' examples were divided into two sets: one used to train the induction algorithms and the second to test their accuracy in predicting gait phases in unseen data. Gait laboratory tests were conducted using three able-bodied volunteers walking on a level floor at speeds from 1.0 - 1.4 m/s in an oval and figure-of-eight walkpath. All data were sampled at 100Hz using a 12 bit analog-digital converter. A gait detectors predictive accuracy was calculated as the fraction of samples for which the correct phase was determined divided by the total number of samples.

2. Summary of Results

The detection accuracy of both induction algorithms was comparable. Rough Sets were computationally more efficient and suitable for real-time operation on small microcontrollers i.e. faster to execute the induced rule base as well as occupying less memory.

Both machine learning techniques outperformed the hand crafted inclinometer detection technique for all three subjects in stance-swing discrimination. The accuracy over the three subjects for the machine learning varied between 94 - 97 % as compared with 87 - 96% for the inclinometer. A difference was noted in the nature of the errors of the two techniques. The errors from the inclinometer method consistently occurred at the phase transitions and typically involved several sequential samples. In the case of machine learning, single sample errors were more randomly distributed over the entire gait cycle. The latter may be clinical less troublesome since the duration of any error condition is greatly reduced.

The machine learning technique was able to determine all five gait phases (an impossible task using the inclinometer technique) with an overall accuracy greater than 82%.

3. Future Work

An implantable version of the accelerometer gait phase detector will be developed for the cat forelimb. A capacitive footfall sensor will also be developed to provide gait phase examples for training and testing the induction detectors. The detection capabilities will also be compared with other machine learning detection schemes based on simultaneously recorded EMG and ENG signals.

B. K. Yoshida and R.B. Stein, University of Alberta

1. Summary of Activities

During this reporting period, we concentrated on modifications to the LIFE design and construction, evaluation of the addition of a shielding wrap on LIFE recordings, and development of a LIFE signal spectral analysis technique.

2. Detailed Description of Activities

After our first implant of LIFEs for this project in NIH20, we evaluated the implant and noted several areas of improvements for future LIFE implants. The primary area to be improved was the 1 hour/electrode implantation time. Analysis of the implantation procedure showed that the actual implantation of the LIFE into the nerve took less than 2 minutes. The balance of the hour was spent anchoring the LIFE's fine wires to the nerve with multiple anchor sutures. The large number of anchors reduced the fine wire to tissue coupling stress and mechanically stabilized the electrode. LIFEs were modified by building strain relief into the electrode, reducing the number of anchor sutures, and modifying the anchor suture attachment. The net result was simplified electrode construction, simplified implant and reduced implant time. Modified electrodes were used in the two LIFE implants in the last quarter of year one. Implant times range between 20 - 30 minutes/electrode and electrode construction time was cut in half. Furthermore, the modified design diverts stress from the fine wires, so greater electrode durability should result. Neural recording performance was not compromised by the change in design.

Recordings were made from LIFEs implanted in forearm showed a significantly greater amount of EMG contamination than recordings from LIFEs in nerves of the hindlimb. An explanation of the difference is the difference in the proximity of the nerve to skeletal muscle. Anatomically, Ulnar and Median nerves are much closer in proximity to skeletal muscle compared tibial nerve. Furthermore, implants in the Tibial nerve in the popliteal fossa eventually are encapsulated by fat, further insulating the electrode from surrounding active muscle. One method to electrically distance electrodes from active muscle is to wrap the implant site with a shield, either insulating or conductive. Implants in NIH23 were made with the addition of flexible implantable shielding material being developed at the University of Alberta. Recordings of LIFEs implanted with insulative shielding showed little to no difference as compared with no shielding. Conductive shielding, however, showed large attenuation of EMG in bipolar LIFE recordings. Monopolar recordings showed, however, that conductive shielding does not attenuate EMG. The shielding changes the shape of the EMG so that EMG contamination in all electrodes within the shielding are the same shape. Thus, differential recordings from bipolar electrodes are able to attenuate EMG through common mode rejection. Development of the shielding material introduces the possibility of augmented lead recordings instead of bipolar recordings. This should result in increased signal to noise ratio and increased recording selectivity.

Analysis of the recorded data has been focused on the spontaneous neural activity and the use of digital signal processing tools to better filter the data, improve signal detection, and evaluate the quality of the recorded signal. Analysis of the power spectral density of LIFEs recordings in acute animals has shown that the signal spectrum lies between 200 Hz and 10 kHz with the peak power density at about 5 - 6 kHz. More recent preliminary data from chronic recordings suggests that the distribution of the spectral density changes with time. The spectrum decreases in amplitude and narrows in bandwidth to lie between 800 Hz and 10 kHz with the peak power density at about 2 kHz and resembles the spectrum from a circumferential cuff electrode in shape. Loss of the high frequency components of this curve are probably due to encapsulation of the electrode, which pushes the active site of the electrode away from the active axons within the nerve.

Analysis to determine the quality of the LIFE recordings has focused on the spontaneous bursts which follow the compound action potential and compound EMG in recordings made with the CAP protocol. During the CAP protocol, the proximal nerve cuff is stimulated supramaximally. This activates muscles in the forelimb which generates motion of the wrist. Mechanoreceptors in the paw and forelimb are activated by this motion and generate a burst of neural activity after the EMG compound. The power of this burst of activity is compared to the power of an equivalent length of time of quiescent spontaneous activity to determine an estimate of EMG free neural activity modulation in the awake animal. The power of the burst also correlates well with peak-to-peak measurements of the CAP, so that it may be possible to relate CAP peak-to-peak measurement with asynchronous neural signal amplitudes.

VII. Appendix A

Abstracts accepted for presentation at the joint IFESS/NP5 Meeting to be held in Vancouver, Canada, August 16-21, 1997.

HOFFERLAB ABSTRACT #1 FOR IFESS/NP5 MEETING:

Multichannel recordings from peripheral nerves: 1. Properties of multi-contact cuff (MCC) and longitudinal intra-fascicular electrode (LIFE) arrays implanted in cat forelimb nerves.

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Motor prostheses for restoring the use of paralyzed hands may benefit from sensory feedback originating from multiple sites, in particular from receptors in individual finger pads. Conventional nerve cuff electrodes provide one channel of sensory information. To obtain multiple sensory nerve channels, three approaches are possible: 1) implant multiple small cuffs on individual digit nerve branches in the hand, 2) implant multiple intrafascicular electrodes in nerve trunks, or 3) implant larger cuffs containing multiple electrodes around nerve trunks. Approach 1) may provide high selectivity but requires delicate surgery and has highest risk of nerve damage. We are investigating approaches 2) and 3) in an animal model and present here preliminary results.

Either 4-channel multi-contact cuffs (MCCs) or, alternatively, sets of four pairs of longitudinal intra-fascicular electrodes (LIFEs) were installed on the left ulnar and median nerves of cats. Conventional recording and stimulating cuffs were implanted distal and proximal to the MCCs or LIFEs, to periodically monitor compound action potential (CAP) shape and amplitude under anesthesia and assess the status of nerves and electrodes over six months.

Implantation of multiple electrodes of either type did not compromise the overall stability of whole-nerve CAP amplitudes (over four months to date). CAP shapes recorded by localized MCC electrodes remained invariant from week to week; CAP amplitudes closely paralleled fluctuations in the whole-nerve CAP but slowly declined after the first month (consistent with expected connective tissue ingrowth). CAPs recorded by LIFEs had complex, variable shapes (suggesting electrode movement) and their amplitudes declined markedly in the first few weeks (suggesting encapsulation) but then started to stabilize. These results suggest that both approaches are safe and may be clinically viable.

HOFFERLAB ABSTRACT #2 FOR IFESS/NP5 MEETING:

Multichannel recordings from peripheral nerves: 2. Measurement of selectivity

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b. School of Engineering Sci., Simon Fraser Univ., Burnaby, BC, V5A 1S6, Canada

Methods for selective recording from nerves and muscles have existed for decades but there is no widely accepted method to measure their selectivity. We have developed a quantitative measure of the selectivity of multi-contact cuff (MCC) nerve recording electrodes and, more generally, of intraneural or extraneural electrode arrays of any type.

In acute experiments under anesthesia, 4-channel MCC electrodes of various designs were placed around cat sciatic nerves in the mid-thigh region. Sets of compound action potentials (CAPs) were recorded in response to stimulating each of 5-8 isolated sciatic branches. Features of CAPs in each data set were used to form a vector in a feature space containing all feature vectors for all nerve branches. Feature vectors were normalized to unitary magnitude. Euler distances were used to measure the differences between normalized vectors in the feature space. MCC electrode selectivity was defined as the average Euler distance between all normalized feature vectors in the feature space.

The measured selectivity indices of acutely implanted 4-channel MCC electrodes of various designs ranged from 11% to 37% of maximum theoretical selectivity. Selectivity was found to depend importantly on regional nerve fiber distribution, cuff dimensions, cuff geometry, number of electrodes and electrode placements within the cuff.

This selectivity index method has application in optimizing electrode designs, monitoring selectivity trends in long-term implants (Strange et al., this meeting) and determining selectivity of nerve recordings in response to mechanical inputs to individual digits (Christensen et al., this meeting).

HOFFERLAB ABSTRACT #3 FOR IFESS/NP5 MEETING:

Multichannel recordings from peripheral nerves: 3. Evaluation of selectivity using electrical stimulation of individual digits.

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We present here initial selectivity measurements for two types of permanently implanted nerve recording electrode arrays, multi-contact cuff (MCC) electrodes and longitudinal intra-fascicular electrodes (LIFEs).

The left median and ulnar nerves of four cats were each instrumented with either 4-channel MCCs or four pairs of LIFEs, as well as with conventional single-channel recording cuffs. Each cat is being studied for at least six months.

In experiments under anesthesia repeated every 1-4 weeks, the nerves supplying each of the five digits were stimulated with external circumferential electrodes placed around the digit, using 10 mA, 50μs pulses. Five sets of eight channels of evoked nerve CAP data were collected each day. The peak-to-peak amplitude of each evoked CAP was determined from averages of ten trials. The sets of CAP amplitudes were analyzed by applying the Euler distance method (Chen et al., this conference), resulting in maximum overall selectivity indices of 61 for MCCs and 75 for LIFEs (theoretical maximum= 100). In comparison, the selectivity indices obtained by using the two single-channel tripolar cuffs placed on the two nerves were in the order of 40.

For repeated measurements over time, selectivity indices declined somewhat in one cat (this is attributed to malfunction of some electrodes) but remained stable in three other cats, indicating that selectivity is an inherent property of an electrode array and its position with respect to the nerve.

These preliminary results suggest that acquiring multi-dimensional sensory information from peripheral nerves may result in useful state feedback for FES applications.

HOFFERLAB ABSTRACT #4 FOR IFESS/NP5 MEETING:

Multichannel recordings from peripheral nerves: 4. Evaluation of selectivity using mechanical stimulation of individual digits.

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Companion studies (Chen et al., Strange et al., this meeting) focused on determinations of nerve recording selectivity using electrical stimulation. Here we investigated the selectivity of recordings using the same cats equipped with chronically implanted MCC or LIFE electrode arrays, but in response to mechanical stimulation of individual digit pads.

A computer-controlled digit manipulator generated two types of mechanical perturbation: brief indentations normal to a digit pad lasting 50 msec or fast slips along that pad, delivered four times/s. Cats were anesthetized for recording sessions. We recorded eight channels of electroneurographic (ENG) activity with electrode arrays and two ENG channels with conventional cuffs. Data were digitized, rectified and filtered to obtain smoothed envelopes of the neural activity profiles in response to mechanical stimulation of the five digits with both perturbation types. Features of the envelopes were used to form the array of feature vectors from which selectivity was measured.

Selectivity for mechanical inputs produced good results with index values up to 60%, about equivalent to results obtained with electrical digit stimulation. However, a large standard deviation was associated with mechanical results, that we did not see with electrical stimulation. This large standard deviation was possibly due to variability in the mechanical inputs, in receptor responses to the inputs, and/or to low signal-to-noise ratio of the neural recordings. More advanced filtering and processing may lead to reduced variability in these data.

We conclude that arrays of implanted nerve electrodes may be used to detect multidimensional sensory inputs applied to digits, suitable for control of multichannel motor prostheses with FES.

HOFFERLAB ABSTRACT #5 FOR IFESS/NP5 MEETING:

Morphometric analysis of cat median nerves after long-term implantation of nerve cuff recording electrodes

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This study aims at quantifying the effects on axons of chronic implantation of tripolar nerve cuff recording electrodes. Four cat median nerves implanted for 6-12 months will be compared to unoperated contralateral control nerves.

Fresh nerve samples were immersed in Karnovsky's fixative, dehydrated, osmicated and embedded in Jembed 812. Sections cut with a glass knife were counterstained. Sample origins were coded to blind the investigators. High-magnification video images were digitized and analyzed using Optimas, a semiautomatic image analysis system that traces outlines of axons but
allows operator intervention when needed.

Axon diameter, fiber (axon plus myelin) diameter, axon circumference, fiber circumference, myelin thickness and g-ratio (axon diameter divided by fiber diameter) are used as morphometric indicators of nerve integrity. This study includes all axons >2 µm in the entire nerve cross section (rather than relying on sampling techniques of questionable accuracy) to investigate whether damage occurred selectively in particular cross-sectional zones of a cuffed nerve.

Compound action potential (CAP) data, collected from cuffed nerves over the period of each implant, will be compared to postmortem morphometric findings to investigate whether the declines in CAP seen in two nerves were associated with a) a net loss of axons, b) a general reduction in axon or fiber diameter, c) selective atrophy of axons near the nerve periphery, d) changes in myelin thickness, or combinations of these factors.

Morphometric analysis of coded samples is still ongoing, thus preliminary results are not available. Full results will be presented at the meeting.

HOFFERLAB ABSTRACT #6 FOR IFESS/NP5 MEETING:

Sensory feedback for control of reaching and grasping using functional electrical stimulation

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We investigated, in an animal model, whether sensory feedback from cuff electrodes can provide state control of FES to restore reaching and grasping in paralyzed limbs.

Three cats were trained to grasp a joystick with the left forepaw, move it toward the mouth and hold it. Once trained, the cats were implanted with tripolar cuff recording electrodes on radial and median nerves and EMG electrodes in 4-6 forelimb muscles.

Two servomotors independently controlled joystick fore-aft stiffness and lateral position. Occasional perturbations in each dimension caused either load changes or slips away from the paw. Cats detected these changes and adjusted their motor output.

EMG recordings showed that individual muscle activation profiles were very consistent and reproducible over trials and days. Averaged EMG profiles were closely represented by simple piecewise-linear envelope functions. ENG signals contained primarily cutaneous information from digits and paw. ENG profiles consistently included recognizable features during phases of
reach and grasp and in response to slip perturbations. An off-line, rule-based threshold detection algorithm was derived that used two sensory ENG channels as input and provided accurate predictions of actual EMG burst features for two flexor muscles.

We envision that in applications of this approach, statistically derived EMG envelope functions may provide templates to synthesize appropriate FES patterns for each paralyzed muscle and sensory nerve recordings may be used as feedback sources for real-time control of muscle stimulation onset, timing and amplitude.

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